IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Attila T. Lorincz, et al.	Group Art Unit: 1634
Serial No	:	09/970,477	Examiner: Johannsen, Diana B.
Filed	:	October 4, 2001	
For	:	ASSESSMENT OF HUMAN PAPILLOMA VIRUS-RELATED DISEASE	

DECLARATION UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is a Declaration under 37 C.F.R. §1.132 by Dr. Attila T. Lorincz in the above-identified application.

I, the undersigned, Attila T. Lorincz, declare and state that:

1. I am a co-inventor of the subject patent application having serial no. 09/970,477.

2. My education and professional experience as an expert in the area of nucleic acid chemistry and analysis are set forth on the attached copy of my Curriculum Vitae.

3. As stated on my Curriculum Vitae attached herewith, my area of expert training and experience is in nucleic acid chemistry, in the analysis of nucleic acids in biological samples, and in the use of such nucleic acid analyses to develop diagnoses and prognoses concerning diseases related to the organism from which the nucleic acid was obtained.

4. I have read and understand the February 13, 2003 Official Action issued in the above-identified case. In particular, I understand that the Examiner has rejected claims 8-12 because the Examiner contends that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. As a person skilled in the art, I respectfully disagree with the Examiner's rejection.

2. As shown by the evidence below, there is a strong and universally accepted correlation between the cell culture models of the specification and diseases in patients.

3. Infection with human papillomavirus (HPV) has been confirmed to be the cause of virtually all cases of cervical cancer (*see*, for example, Walboomers, et al., *J. Pathol.* 189:12, 1999; **Exhibit 1**) and has been identified in a high percentage of non-melanoma skin cancers, in cancers of the oral cavity, the larynx, and the esophagus, in intraepithelial neoplasias and in various type of hyperkeratoses (*see*, for example, zur Hausen, *Biochimica et Biophysica Acta* 1288:F55, 1996; **Exhibit 2**). In fact, HPV is associated with a spectrum of lesions ranging from benign epithelial hyperproliferation to invasive carcinomas. For example, viral gene expression of HPV is tightly linked to cellular differentiation. (*See* Broker et al. *Cancer Cells*, 7:197, 1989; **Exhibit 3**). *See* also Southern and Herrington (*Sex. Transm. Inf.* 74:101, 1998; **Exhibit 4**) who describe that human papillomavirus has been identified as the major aetiological factor in cervical carcinogenesis. In addition, Stoler (*Int. J. Gynecol. Pathol.* 19:16, 2000; **Exhibit 5**) describes human papillomaviruses as the etiologic agents of cervical neoplasia.

4. The zur Hausen publication describes HPV types 1 through 70 and the human pathology related to infection with each type of HPV. The Walboomers publication describes the worldwide HPV prevalence in 99.7% of cervical carcinomas.

5. However, most human papillomavirus infections resolve spontaneously without causing cancer or development of cancer precursors. Therefore, it is useful to be able to distinguish those infections that may progress to cancer from those that may resolve spontaneously. Furthermore, it is useful to employ treatments early that may be effective in preventing and/or treating the human papillomavirus infection in the pre-cancerous stage so that the progression to cancer can be inhibited.

6. Generally, human papillomaviruses cannot be cultured *in vitro*, although HPV type 16 has been cultured *in vitro* with limited success. Therefore, model systems for human patients have been developed to study the stages of HPV infection and their relationship to the development of HPV-induced neoplasia and cancer.

7. Cell lines such as HaCaT, W12, and SiHa are universally recognized by researchers as model systems of human epithelium in a patient at various stages progressing to cancer. These human cell lines contain different HPV copy numbers per cell and are used to model different stages of HPV-induced neoplasia and cancer in human patients. For example, the HPV negative cell line, HaCaT, is an immortalized cell line that is useful as a

model system. Cultures of HaCaT cells, transfected by HPV 16 DNA that are in the episomal form, represent a useful model of early HPV infection typical of a non-neoplastic lesion. Cell lines that contain an increased amount of HPV in an episomal form, such as W12, represent a pre-malignant condition in humans. Cell lines that contain HPV in an integrated form, such as SiHa, represent relatively advanced human cancer.

8. The HaCaT cell line is a naturally immortalized human keratinocyte cell line similar in some ways to W12. (*See* Boukamp et al., *J. Cell Biol.*, 106:761, 1988. **Exhibit 6**). HaCaT cells correlate to human epithelium, in particular, keratinocytes, and are used to model human disease in a patient. Thus, HaCaT cells infected with HPV represent human patient epithelium infected with HPV. The Boukamp article describes HaCaT as the first permanent epithelial cell line from adult human skin that exhibits normal differentiation and provides a promising tool for studying regulation of keratinization in human cells. The cell line maintains full epidermal differentiation capacity and remains nontumorigenic even when transplanted onto nude mice. (*See* Abstract). The Boukamp article concludes that "the HaCaT cell line is closely approximated to normal keratinocytes, and thus offers a suitable model to study regulatory mechanisms in the process of differentiation of human epidermal cells....This cell line provides a valuable model system for the study of the role of oncogenes and other factors in the process of malignant conversion of human epithelial cells." (*See* page 770, last paragraph).

9. White et al. (*J. Virology*, 72:959, 1998; **Exhibit 7**) describes the infection of HaCaT cells with HPV virions extracted from HPV-infected human condylomas. The HPV-infected HaCaT cells were xenografted onto mice in order to test neutralizing antibodies prepared as part of an HPV vaccine development program. The White article states that based on this model system, an *in vitro* assay which can be used to study the early stages of HPV-16 infection was developed. (*See* page 962, right hand column). Thus, this study further demonstrates the usefulness of the HaCaT cell line as a model for early stage HPV infection.

10. The W12 cell line, which contains HPV in an episomal form, correlates to human epithelium, in particular, keratinocytes, and is used to model premalignant human disease. Coleman, N. and Stanley, M. A.(*Hum. Pathol.* 25:73-79, 1994; **Exhibit 8**) describe the cervical keratinocyte cell line W12 as a model for low-grade squamous intraepithelial lesions and that the SiHa and CaSki cell lines are models for high-grade squamous intraepithelial lesions and cancers. (*See* Abstract).

11. Coleman and Stanley conclude that "differential expression patterns in cervical keratinocytes *in vivo* are mirrored by the *in vitro* finding that L1 is only patchily present in the high-grade epithelium produced by CaSki and SiHa cells, but is strongly expressed in differentiated layers of NCx [normal cervix] and W12 cells." (*See*, pg. 78, col. 1-2). Thus, Coleman and Stanley establish a strong correlation between the W12 and SiHa cell lines and human patients.

12. SiHa cells which contain HPV integrated into the genome correlate to human epithelium, in particular, keratinocytes, and are used to model malignant human disease. Rong, et al. (*Chinese Medical Journal* 109:854, 1996; **Exhibit 9**) describe the use of CaSki, SiHa, HeLa, and W12 cell lines in determining the susceptibility of HPV-infected keratinocytes to lysis by specific cells generated by the immune system. The authors describe the cell lines as follows:

13. "Cervical carcinoma derived keratinocytes, CaSki (HPV16+, 300-500 copies), SiHa (HPV16+, 1 copy) and HeLa (HPV18+, 100 copies), were maintained in continuous culture in Glasgow's modification of Eagle's medium (GMEM) containing 10% FCS at 37 °C in a 5% CO_2 incubator. They were used as models of high grade squamous intraepithelial lesion (HSIL) according to the Bethesda system." (Rong, et al. Page 855, col. 1, 2nd complete par.; emphasis added).

14. "W12, as a model of low grade squamous intraepithelial lesion (LSIL), is a cervical keratinocyte line which is immortalized but non-transformed by natural infection with HPV 16....It contain[s] about 100 copies of HPV 16 DNA in the episomal form." (Page 855, col. 1, 3rd complete par.; emphasis added).

15. Thus, Rong, et al. establish that cell lines such as CaSki, HeLa, HaCaT, W12, and SiHa are universally recognized by researchers as model systems of human patient epithelium at various stages progressing to cancer.

16. Tan and Ting, (*Cancer Research* 55:4599, 1995; **Exhibit 10**) correlate the response of SiHa and CaSki cell lines to the response of SiHa-induced human tumors in nude mice when treated with phosphorothioate oligonucleotides. HPV RNA was measured in CaSki cells and in the tumor cells extracted from the mice before and after treatment. The results demonstrated that treatment with the antisense oligonucleotides resulted in the reduction of HPV RNA expression levels in both the CaSki cells and the mouse tumors, in the inhibition of CaSki and SiHa cell proliferation, and in the inhibition of mouse tumor growth.

17. Madrigal, et al. (*Gynecol Oncol*, 64:18, 1997; **Exhibit 11**) report reducing the expression of the HPV oncogenes with phosphorothioate oligonucleotides in cervical cancer cells. In this publication, SiHa, CaSki, and HeLa cell lines were used as models of cervical cancer and the results were shown to be consistent with similar experiments that used cells cultured from primary cervical tumors. The IC_{50} data obtained from the SiHa and CaSki cells and the primary cervical tumor cells were virtually identical. These data demonstrate the usefulness of SiHa and CaSki cells lines as models for human cancer.

18. Additionally, Z. Naghashfar, et al. (*Cancer Letters* 100:47-54, 1996; **Exhibit 12**) describe prostate tumor progression models where HPV 16 DNA and HPV 18 DNA are used to immortalize human prostate epithelial (HPE) cells. The human prostate epithelial (HPE)/HPV immortalized cell lines are useful as a model for examining the effects of therapeutic agents for treating androgen-independent prostate tumor cells. Detection of HPV 16 and 18 sequences were confirmed with positive controls SiHa cell DNA and HeLa cell DNA, respectively. HeLa cells are human cervical carcinoma cells derived from keratinocytes and are useful as a model system for human disease.

19. Koromilas, et al. (*Cytokine & Growth Factor Reviews* 12:157-170, 2001; **Exhibit 13**) report that the HPV is the infectious agent in cervical neoplasia where the major risk factors are high risk HPV types 16, 18, 31, 33, 35, 39, and 41-45. The review also states that "the only viral genes which are consistently expressed following integration is the E6 and E7 oncogenes and these genes are critical for the development of malignant transformation and also play a role in altering the cellular response to cytokines" (page 158, col. 1, 2nd par.). Koromilas, et al. associate the various HPV types and HPV genes, such as E6, E7, E5, E4, E2, E1, L1, and L2, to transformation and disease.

22. These are but a few examples of a wide body of literature that support the use of HPV-containing cell lines as models of human cancer and the widespread use of these cell lines to investigate potential preventive and therapeutic treatments for human cancer patients.

23. As shown by the evidence below, there is a correlation between HPV transcripts and various disease stages. For example, Mark H. Stoler (*Intl. J. Gyn. Path.* 19:16-28, 2000; **Exhibit 5**) supports the association of CIN1 and CIN3 or invasive squamous cancers with HPV types. Infection by HPV types 16, 18, 31, and 45 accounts for almost 80% of the invasive cervical cancers (pg. 19, col. 2, par. 2). Stoler further indicates that "active transcription of HPV DNA within lesions establishes a strong molecular association of HPV with cervical neoplasia" (pg. 20, col. 1, par. 2). In addition, this publication describes using

HPV DNA and HPV mRNA expressed in lesions to identify patterns of viral expression, where "the presence of viral RNA and protein expression leads to a rational framework implicating the virus in lesion pathogenesis. Patterns of viral mRNA expression vary with morphology in a tightly regulated and differentiation-dependent manner" (pg. 20, 1st col., par. 1) where low-grade lesions do not have a restricted pattern of viral gene expression as found in invasive cancer. These reviews associate HPV types to cervical neoplasia, HPV genes to transformation and disease, and correlate HPV nucleic acid expression to lesion pathogenesis.

24. Saewha Jeon and Paul F. Lambert (*PNAS* 92:1654-1658, 1995; **Exhibit 14**) demonstrate that integration of HPV 16 DNA leads to increased steady-state levels of mRNAs encoding the viral oncogenes E6 and E7. Jeon and Lambert also report that expression of E6 and E7 genes in transgenic mouse systems leads to tumor formation (pg. 1654, col. 1, par. 1). This publication demonstrates the correlation of HPV gene expression, *i.e.*, E6 and E7 mRNA measurements, and disease, such as cervical cancer.

25. Goodwin and DiMaio (*PNAS* 97(23):12513-12518, 2000; **Exhibit 15**) describe that HPV 18 transcript ratios are associated with transformation, cancer, and disease stage. In particular, Goodwin and DiMaio establish that HPV 18 is associated with cervical cancer. To demonstrate the association between HPV 18 transcript measurements with transformation and disease, the authors use the HeLa cell line as a model for HPV 18-induced cervical carcinoma. Goodwin and DiMaio describe repression of HPV 18 E6 and E7 expression by inducing E2 expression, resulting in increased p53 and pRB, leading to tumor suppression. Goodwin and DiMaio correlate E6/E7 expression and the tumor suppressor pathways, p53 and Rb, in HeLa cells (page 12517 "Implications"). The abstract states that "most cervical carcinomas express high-risk human papillomaviruses (HPVs) E6 and E7 proteins, which neutralize cellular tumor suppressor function." Since Goodwin and DiMaio report that repression of HPV oncogenes in HeLa cervical carcinoma cells induces tumor suppression, one skilled in the art understands from reading the instant application and this reference that HPV transcript measurements are associated with transformation, cancer, and disease stage.

26 Thus, it is my experience and my opinion, as one skilled in the art of HPV-induced disease, diagnosis, and treatment, that cell lines such as, but not limited to, HaCaT, W12, and SiHa are universally recognized by researchers as model systems of human epithelium at various stages of progression to cancer. It is also my opinion that the experimental results disclosed in the above-identified specification correlate to HPV-induced

neoplasia, disease and cancer in humans and correlate to the diagnosis of risk, onset and stage of HPV-induced neoplasia, disease and cancer in humans. Furthermore, it is my opinion that one skilled in the art understands how to make and use the instant invention from the prior art and the instant specification.

27. It is also my opinion, as an expert in the field of nucleic acid chemistry analysis and inventor of several patents related to the use of HPV types in diagnostic testing (U.S. Patent Nos. 4,849,331, 4,849,332, 4,849,334, 4,908,306 and, 6,355,424), that the methods in the above-identified application are enabled as described in the instant specification and as commonly understood in the art.

28. To support this position, I present evidence herein establishing that the method described in the instant specification in relation to HPV 16, also applies to other HPV types, such as HPV 18 and HPV 31. The data provide expression model systems for HPV 18 and HPV 31 using the E6-E7/L1 mRNA ratio assessment. The skilled artisan understands from reading the instant specification how to assess risk, onset, and stage HPV-induced disease in humans using other HPV genes, such as E4, E5, L2, etc.

29. The following experimental study describes an HPV 18 mRNA expression model for assessing the E6-E7/ L1 mRNA ratio. HPV 18 single-stranded DNA probes specific for E6-E7 and L1 regions were designed and developed using established protocols. HPV 18 E6-E7 and L1 RNA, complementary to the DNA probes, were transcribed *in vitro* and used as the calibrator for normalization. The expression analysis system (EAS) protocol was utilized to obtain the expression data. The HPV 18 E6-E7/L1 mRNA ratio was measured in the HPV 18 positive human cervical carcinoma cell line, HeLa (ATCC, Manassas, VA).

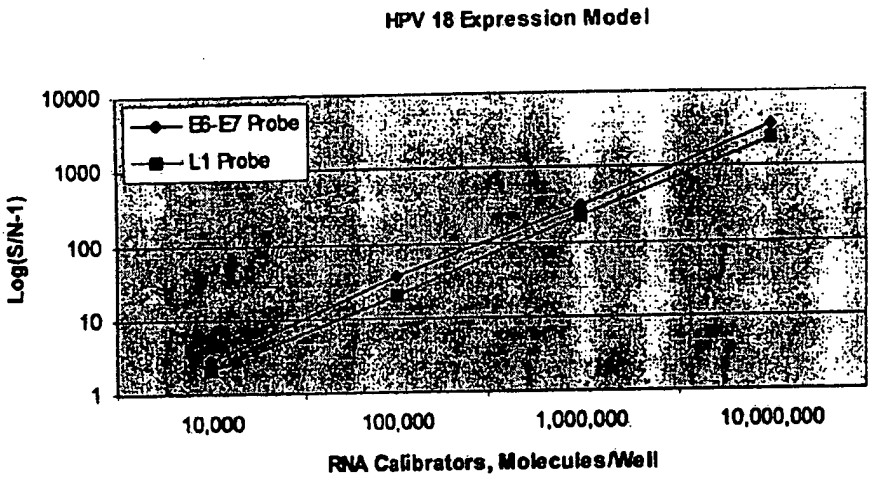
30. DNA probes were developed using PCR amplification and λ Exonuclease digestion. The following PCR primer pairs were used, where the HPV 18 E6-E7 and L1 probe sequences correspond to nucleotide regions 148-843 and 5748-6720 of the HPV 18 genome, respectively.

E6-E7 region	L1 region
5'-CTGATCTGTGCACGGAACTG-3'	5'-GGTAATCCATATTTTAGGGT-3'
5'-GCTCGAAGGTCGTCTGCT-3'	5'-CCTCAACATGTCTGCTATAC-3'

31. *In vitro* transcribed HPV 18 E6-E7 and L1 RNA were quantified and used as the calibrator for the model system. HPV 18 RNA calibrators were used at 10^3, 10^4, 10^5, 10^6, and 10^7 molecules per well.

32. The assay uses normal human keratinocytes (BioWhittaker, San Diego, CA) and HeLa cells, where 10,000 cells per well were lysed with Proteinase K (50 units per well) for 30 min at 37°C. The mixture of HPV 18 RNA calibrators, cell lysates, and DNA probe (E6-E7 or L1 at 180 pM) in hybridization buffer (Digene) was hybridized for 2 hours at 65°C. RNA/DNA hybrids were captured onto streptavidin-coated plates (Digene) for 1 hour at room temperature with agitation at 1100 rpm. Captured RNA/DNA hybrids were recognized by anti-RNA/DNA hybrid antibodies (DR-1, Digene). Incubation with DR-1 was performed for 30 min at room temperature. The plate was washed with HCII Wash buffer (Digene) 4 times, incubated with Enhance buffer (Digene) for 45 min at 53°C, and washed again 4 times with HCII Wash buffer. The plate was incubated with DR-2 (Digene) for 15 min at room temperature, and then read on a luminometer. HPV 18 negative normal human keratinocytes were used as a background signal (N; Noise) to assess the HPV E6-E7 and L1 mRNA levels measured from HPV 18 positive HeLa cells. Both cell lines were used at the same concentrations, 10,000 cells/well.

GRAPH 1



RNA Calibrators, Molecules/Well	10,000	100,000	1,000,000	10,000,000
E6-E7 Probe, S/N-1	2.7	37.3	306.4	3549.7
L1 Probe, S/N-1	2.1	20.6	219.8	2404.3

Table 1. HPV 18 Expression Model: The analytical sensitivity of the HPV 18 probes is depicted in Graph 1 and Table 1 ($intercept_{E6\text{-}E7}$= -5.14, $slope_{E6\,E7}$=1.28; intercepts=-3.85, $slopes_{L1}$=1.03).

Cells, 10,000 per well	Average Negative RLU (Keratinocytes)	Average Positive RLU (HeLa)	%CV	S/N	Total mRNA	mRNA/cell
E6-E7	79	53,988	6.1	683.4	1,749,217	175
L1	153	6,142	26.5	40.1	184,963	18

Table 2. HPV 18, E6-E7 and L1 mRNA in HeLa: HPV 18 E6-E7 and L1 mRNA detection using the HeLa cell line. The assay was run in triplicate.

Cell Line	E6-E7/L1 Ratio
HeLa	9.5

Table 3. The HPV 18 E6-E7/L1 mRNA Ratio.

33. The E6-E7/L1 mRNA ratio was found to be 9.5 for HPV 18 positive human cervical carcinoma cell line HeLa. This E6-E7/L1 mRNA ratio correlates to the claimed invention, i.e. This ratio represents substantially higher expression of the carcinogenesis-related genes E6-E7 than the viral capsid structural L1 gene.

34. As further evidence that the claimed HPV gene transcript ratio applies to other HPV types, an HPV 31 mRNA expression model was developed for the E6-E7/L1 mRNA ratio assessment. HPV 31 single-stranded DNA probes specific for E6-E7 and L1 regions were designed and developed using established protocols. Full-length HPV 31 RNA, complementary to the DNA probes, was transcribed *in vitro* and used as the calibrator for normalization. The EAS protocol was utilized to obtain the expression data. The HPV 31 E6-E7/L1 mRNA ratio was measured in total cellular RNA isolated from the HPV 31 positive neoplastically transformed cell lines LKP31 and A31 (a gift from Dr. L.A. Laimins, Northwestern University).

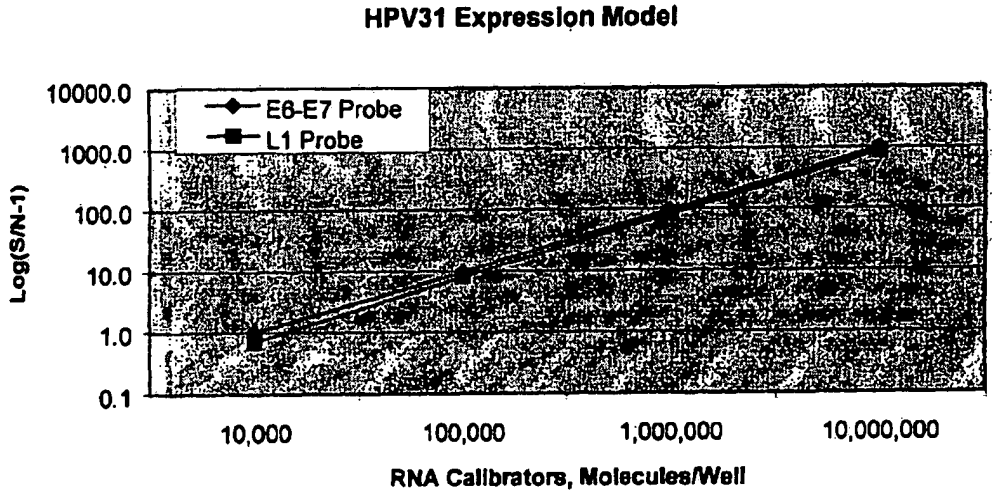
35. DNA probes were developed using PCR amplification and λ Exonuclease digestion. The following PCR primers pairs were used, where the HPV 31 E6-E7 and L1 probe sequences correspond to nucleotide regions 96-803 and 5964-7017 of the HPV 31 genome, respectively.

E6-E7 region	L1 region
5'-CCTACAGACGCCATGT-3'	5'-GTGGTCCTGGCACTGATAAT-3'
5'-GCTCTTGCAATATGCGAATA-3'	5'-GGGTGCACTACGTTTACCTG-3'

36. *In vitro* transcribed full-length HPV 31 RNA was quantified and used as the calibrator for the model. HPV 31 RNA calibrators were used at 10^4, 10^5, 10^6, and 10^7 molecules per well.

37. The assay uses a mixture of HPV 31 RNA from the calibrators or isolated from cell lines and DNA probe (E6-E7 at 360 pM and L1 at 1500 pM) in hybridization buffer (Digene). Hybridization occurred for 2 hours at 65°C. RNA/DNA hybrids were captured onto streptavidin-coated plates (Digene) for 1 hour at room temperature with agitation at 1100 rpm. Captured RNA/DNA hybrids were recognized by anti-RNA/DNA hybrid antibodies (DR-1, Digene). Incubation with DR-1 was performed for 30 min at room temperature. The plate was washed with HCII Wash buffer (Digene) 4 times, incubated with Enhance buffer (Digene) for 45 min at 53°C, and washed again 4 times with HCII Wash buffer. The plate was incubated with DR-2 (Digene) for 15 min at room temperature, and then read on a luminometer. The total cellular RNA samples, isolated from human keratinocytes were transfected with HPV 31 DNA. Both cell lines utilized in this assay, LKP31 and A31, contained episomal and integrated copies of HPV 31 DNA; however, LKP31 had a higher copy number than A31, and thus LKP31 is assumed to represent a cell line that is closer to cancer. E6-E7 and L1 mRNA expression analysis was performed using 500 ng per well of the cellular RNA sample. The 500 ng of total RNA approximately corresponded to $1.4x10^4$ cells (based on Qiagen RNeasy Handbook, 35 µg of total RNA ~ 10^6 cells, and Digene experimental data, 32 µg of total RNA $2x10^6$ cells).

Graph 2



RNA Calibrators, Molecules/Well	10,000	100,000	1,000,000	10,000,000
E6-E7 Probe, S/N-1	1.0	9.6	95.2	1007.1
L1 Probe, S/N-1	0.7	8.0	81.4	861.2

Table 4. HPV 31 Expression Model: The analytical sensitivity of the HPV 31 probes is depicted in Graph 2 and Table 4 ($intercept_{E6\text{-}E7}$= -4.05, $slope_{E6\text{-}E7}$=1.01; $intercepts_{L1}$=-4.23, $slopes_{L1}$=1.02).

Total RNA 500 ng/well	Average Negative RLU	Average Positive RLU	%CV	S/N	Total mRNA	mRNA/cell
LKP31	36.3	25,836	25.7	711.1	7,186,810	513
A31	36.3	11,174	1.0	307.5	3,120,083	223

Table 5. HPV 31 E6-E7 mRNA. Specimens were tested in duplicate.

Total RNA 500 ng/well	Average Negative RLU	Average Positive RLU	%CV	S/N	Total mRNA	mRNA/cel l
LKP31	51.7	2,615	14.8	50.6	612,792	44
A31	51.7	1,584	0.3	30.7	370,737	27

Table 6. HPV 31 L1 mRNA detection using the LKP31 and A31 total RNA samples. Specimens were tested in duplicate.

Cell Line	E6-E7/L1 Ratio
LKP31	11.7
A31	8.4

Table 7. The HPV 31 E6-E7/L1 mRNA Ratio.

38. The E6-E7/L1 mRNA ratio was found to be above 2 for both HPV 31 positive cell lines LKP31 and A31. This ratio represents higher expression of the carcinogenesis-related genes E6-E7 than the viral capsid structural L1 gene. The levels of E6-E7 and L1 mRNA were approximately 2-fold higher in LKP31 cells than in the A31 cells. The higher level of E6-E7 to L1 is expected in cells that are transformed by HPV 31 to the pre-malignant state, and as expected, the more neoplastic cell line LKP31 had a higher ratio of E6-E7 to L1.

These experiments demonstrate that HPV gene transcript ratios of different HPV types, *i.e.*, HPV 18 and HPV 31, may be used to determine the disease level in cell model systems of HPV-infected cells. In particular, the expression levels of E6-E7 and L1 mRNA were detected; however, one skilled in the art may, from reading the instant specification, determine the HPV gene transcript ratio of other HPV genes than E6-E7 and L1.

39. The cell lines such as HeLa, W12, SiHa are widely recognized by scientists as model systems of human epithelium in a patient at various stages progressing to cancer, where these cell lines contain different HPV copy numbers per cell. It is my opinion that the instant specification and prior art at the time of filing enables one skilled in the art to

diagnose and prognose a patient having an HPV-induced disease using HPV gene transcripts as an indicator. In addition, the specification teaches and provides guidance for the skilled artisan to measure and analyze HPV gene transcript ratios for diagnosis of disease caused by different HPV types.

40. I declare further that all statements made on information and belief are believed to be true, and, further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and such willful false statements may jeopardize the validity of the instant patent specification or any patent issuing thereon.

Respectfully submitted,

Date: June 12, 2003

Attila T. Lorincz, Ph.D.

Curriculum Vitae

ATTILA T. LÖRINCZ, PH.D.

Address: **Work:** Digene Corporation
1201 Clopper Road
Gaithersburg, MD 20878
Phone: 301-944-7350
E-mail: ATTILA.LORINCZ@DIGENE.COM

Home: 6 Chinaberry Court
North Potomac, MD 20878
Phone: 301-869-2404

University Education:

Graduate, 1976-1979 Department of Genetics, Trinity College, Dublin, Ireland.
Ph.D., 1980. Research project: Investigation of cell size and cell division control in *Saccharomyces cerevisiae.*

Undergraduate, 1972-1976 University College, Dublin, Ireland.
B.Sc., Honors 1976. Microbiology (major), Biochemistry (minor).
Research project: Characterization of an α-amylase of *Pseudomonas saccharophila.*

Professional Positions:

Senior Vice President and Chief Scientific Officer, since 2000. Digene Corporation, Gaithersburg, Maryland 20878.
Report directly to company President and CEO. Responsibilities include: key role in company policy decision-making at the executive committee level; speaking at scientific meetings worldwide as an acknowledged expert on human papillomaviruses and genetic testing; instigating and supervising basic scientific research; collaborating with scientists worldwide in studies published in prestigious peer-reviewed journals; evaluating Digene's position on intellectual property; evaluating new technology in other laboratories for possible licensing or other use by Digene; representing Digene and its technology at business meetings worldwide.

Vice President, R&D, and Scientific Director, 1990-1999:
Responsibilities included: supervision and guidance of up to 40 scientists, long-range scientific planning for the company, review of detailed research plans, assurance of quality results, and timely achievement of company R&D goals. Principal areas of research focus were the development of diagnostic nucleic acid probe tests for a broad range of human infectious diseases, cancers, and inherited disorders. Other responsibilities included the planning and coordination of clinical studies, U.S. Food and Drug Administration submissions, and interactions with high-level biomedical consultants and collaborators from universities and other companies.

Lecturer, 1999. Zanvyl Krieger School of Arts and Sciences, Johns Hopkins University, Montgomery County Center, Rockville, MD 20850.
Designed and taught a new course in the history of medical diagnostics for candidates for the M.A. in Biotechnology.

Adjunct Associate Professor, 1989-present. Department of Pathology, Georgetown University Medical School, Washington, DC 20007.
Research efforts focused on human papillomaviruses, with particular emphasis on diagnostic applications, and on molecular mechanisms of carcinogenesis in human keratinocytes. Other projects involved the study of tumor suppressor genes and their use as markers for cancer prognosis.

Scientific Director, Corporate Research, 1989-1990. Life Technologies, Inc., Gaithersburg, Maryland. Studied *in vitro* transcription, transgenic animals, and other model systems of interest to research scientists for the purpose of generating research reagents.

Section Head of Advanced Molecular Diagnostics, 1984-1989. Life Technologies, Inc. Gaithersburg, Maryland. Investigated medical and molecular aspects of the human papillomavirus.

Research Scientist, 1982-1984. University of California at Santa Barbara. Investigated regulation and organization of *S. cerevisiae* genes involved in cell cycle control.

Research Scientist, 1980-1982. University of California at San Diego. Performed quantitative computer analyses of protein regulation during the cell cycle of *S. cerevisiae*, using two-dimensional gel electrophoresis.

Honors And Other Professional Activities:

High Technology Council of Maryland Award for Biotechnology Product of the Year 2000, awarded to the Hybrid Capture® II HPV DNA Test.

American Venereal Disease Association A.V.D.A. Achievement Award 1994, presented in recognition of outstanding contributions toward the control of sexually transmitted diseases.

Primary author of cell cycle paper in Nature, 1984.

Senior author of papers in JAMA, 2000, detailing the role of HPV in cervical cancer screening.

Editorial board member of IVD Technology and of Clinical and Diagnostic Virology.

Scientific and medical reviewer for: Obstetrics and Gynecology, Science, Journal of Clinical Microbiology, Journal of General Virology, Clinical and Diagnostic Virology, and others.

Peer reviewer for the National Institutes of Health, since 1986.

Life Technologies, Inc., David L. Coffin Award for Technical Innovation, for developing the FDA approved HPV test ViraPap®, 1989.

Life Technologies, Inc., David L. Coffin Patent Award, for human papillomavirus 56 nucleic acid hybridization probes and methods for employing same, US Patent No. 4,908,306.

Irish Department of Education Ph.D. Scholarship Recipient, 1976-1979.

National Clinical Trials:

Co-principal investigator for HPV QC Group in the NCI ALTS study to investigate alternatives in women's health care for managing cervical disease. Contract NCI-CN-55044-07, awarded 1995.

Federal Research Grants:

Principal Investigator for Contract N44-AI-85335, "Rapid Detection and Typing of HSV DNA." SBIR Phase II grant from NIAID, awarded May, 1998.

Principal Investigator for Contract N43-AI-45214, "Rapid Detection and Typing of Herpes Simplex virus (HSV) DNA in Clinical Specimens." SBIR Phase I grant from NIAID, completed 1996.

Subcontract MA-5623-26 with Microbiological Associates, Inc., "Assays to Detect and Type Human Papillomavirus DNA in Cervical Lavage Samples." Completed 1995.

Patents:

US patent nos. 4,849,331; 4,849,332; 4,849,334; and 4,908,306 for the use of HPV types 35, 43, 44, and 56 in diagnostic testing.

US patent nos. 5,981,179 and 6,027,897 and Australian patent no. 711130 for CAR target amplification technology.

Australian patent no. 673813 for Hybrid Capture® technology.

Other patents pending for Hybrid Capture® technology.

Memberships:

American Society for Microbiology (since 1980)

Pan American Group for Rapid Viral Diagnosis (since 1986)

American Association of Clinical Chemistry (since 1991)

International Committee on HPV Nomenclature (1986-1991)

International Conferences

Dr. Lörincz has been an invited speaker at many international conferences, a list of which is available on request.

Departmental Seminars

Dr. Lörincz has been an invited speaker at many departmental seminars, a list of which is available on request.

Managerial Experience:

- Head of several scientific teams, with full responsibilities for project planning, budgets, hiring, promotions, data analyses, presentations, publications, etc. Principal Investigator for numerous clinical studies. As a member of the executive staff of Digene, I am intimately involved in setting overall company objectives and policies.
- Head of several multi-disciplinary strategic planning teams involving R&D, Regulatory Affairs, Marketing and Sales, Development, and Manufacturing.
- Director of Intellectual Property for Digene Corporation, 1990-1994. Prepared patent applications with assistance of attorneys.

- Played a major role in preparing several PMA applications for Life Technologies' and Digene's HPV testing kits. Presented data to FDA panels, leading to successful approval of the ViraType® and Hybrid Capture® kits for detecting and typing HPV DNA.

- Key member of the Executive Committee directing a successful initial public offering of Digene Corporation on NASDQ in May, 1996, and a secondary offering in October, 1997.

SELECTED PUBLICATIONS

Dr. Lörincz has 72 peer-reviewed scientific publications prior to 1995, a list of which is available on request. A list of peer-reviewed publication since 1995 follows:

Schiffman, M.H., N.B. Kiviat, R.D. Burk, K.V. Shah, R.W. Daniel, R. Lewis, J. Kuypers, M.M. Manos, D.R. Scott, M.E. Sherman, R.J. Kurman, M.H. Stoler, A.G. Glass, B.B. Rush, I. Mielzynska, and **A.T. Lorincz** (1995) Accuracy and interlaboratory reliability of human papillomavirus DNA testing by Hybrid Capture. J. Clin. Microbiol. 33:545-550.

Cox, J.T., **A.T. Lorincz**, M.H. Schiffman, M.E. Sherman, A. Cullen, and R.J. Kurman (1995) Human papillomavirus testing by hybrid capture appears to be useful in triaging women with a cytologic diagnosis of atypical squamous cells of undetermined significance. Am. J. Obstet. Gynecol. 172(3):946-954.

Reid, R., and **A.T. Lörincz** (1995) Human papillomavirus tests. In: Ballière's Clinical Obstetrics and Gynaecology (H.W. Jones, III, guest ed.), vol. 9, no. 1, pp. 63-103. Ballière Tindall, London.

Lorincz, A. (1995) Hybrid Capture™: A simple, sensitive method for the routine detection of HPV DNA. In: Screening of Cervical Cancer: For Whom, Why and How? Experts' Conference. 2nd International Congress of Papillomavirus in Human Pathology. Paris, France, Unesco, April 6, 7, 8, 1994 (Monsonego, J., ed.), pp. 59-62. EUROGIN Scientific Publications, Paris.

Wideroff, L.; Schiffman, M.H.; Nonnenmacher, B.; Hubbert, N.; Kimbauer, R.; Greer, C.E.; Lowy, D.; **Lorincz, A.T.**; Manos, M.M.; Glass, A.G.; Scott, D.R.; Sherman, M.E.; Kurman, R.J.; Buckland, J.; Tarone, R.E.; Schiller, J (1995) Evaluation of seroreactivity to human papillomavirus type 16 virus-like particles in an incident case-control study of cervical neoplasia. J. Infect. Dis. 172(6):1425-1430.

Lörincz, A. (1995) Human papillomaviruses. In: Diagnostic Procedures for Viral, Rickettsial, and Chlamydial Infections, 7th edition (Lennette, E.H., et al., eds.), pp. 465-480. American Public Health Association, Washington, D.C.

Lörincz, A. (1996) Hybrid Capture™ method for detection of human papillomavirus DNA in clinical specimens. Papillomavirus Report 7(1):1-7.

Reid, R.; **Lörincz, A.** (1996) New generation of human papillomavirus tests. In: Cervical Cancer and Preinvasive Neoplasia (Rubin, S.C.; Hoskins, W.J., eds.), pp. 27-47. Lippincott-Raven, Philadelphia.

Lörincz, A.T. (1996) Molecular methods for the detection of human papillomavirus infection. In: Obstetrics and Gynecology Clinics of North America: The Papillomaviruses, 2nd edition (Lörincz, A.T.; Reid, R., eds.), vol. 23, no. 3, pp. 707-730. W.B. Saunders, Philadelphia.

Tsukui, T.; Hildesheim, A.; Schiffman, M.H.; Lucci, J., III; Contois, D.; Lawler, P.; Rush, B.B.; **Lorincz, A.T.**; Corrigan, A.; Burk, R.D.; Qu, W.; Marshall, M.A.; Mann, D.; Carrington, M.; Clerici, M.; Shearer, G.M.; Carbone, D.P.; Scott, D.R.; Houghten, R.A.; Berzofsky, J.A. (1996) Interleukin 2 production *in vitro* by peripheral lymphocytes in response to human papillomavirus-derived peptides: correlation with cervical pathology. Cancer Res. 56(17):3967-3974.

Hall, S.; **Lörincz, A.**, Shah, F.; Sherman, M.E.; Abbas, F.; Paull, G.; Kurman, R.J.; Shah, K.V. (1996) Human papillomavirus DNA detection in cervical specimens by Hybrid Capture: correlation with cytologic and histologic diagnoses of squamous intraepithelial lesions of the cervix. Gynecol. Oncol. 62:353-359.

Wideroff, L.; Schiffman, M.H.; Hoover, R.; Tarone, RE; Nonnenmacher, B.; Hubbert, N.; Kimbauer, R.; Greer, C.E.; **Lorincz, A.T.**; Manos, M.M.; Glass, A.G.; Scott, D.R.; Sherman, M.E.; Buckland, J.; Lowy, D.; Schiller, J. (1996) Epidemiologic determinants of seroreactivity to human papillomavirus (HPV) type 16 virus-like particles in cervical HPV-16 DNA-positive and -negative women. J. Infect. Dis. 174(5):937-943.

Lörincz, A.T. (1996) Hybrid Capture™ method for detection of human papillomavirus DNA in clinical specimens: a tool for clinical management of equivocal Pap smears and for population screening. J. Obstet. Gynaecol. Res. 22(6):629-636.

Lörincz, A. (1997) Human papillomavirus testing. Pathology Case Reviews 2(1):43-48.

Sherman, M.E.; Schiffman, M.H.; **Lörincz, A.T.**; Herrero, R.; Hutchinson, M.; Bratti, C.; Zahniser, D.; Morales, J.; Hildesheim, A.; Helgesen, K.; Kelly, D.; Alfaro, M.; Mena, F.; Balmaceda, I.; Mango, L.; Greenberg, M. (1997) Cervical specimens collected in liquid buffer are suitable for both cytologic screening and ancillary human papillomavirus testing. Cancer 81(2):89-97.

Sherman, M.E.; Schiffman, M.H.; Mango, L.J.; Kelly, D.; Acosta, D.; Cason, Z.; Elgert, P.; Zaleski, S.; Scott, D.R.; Kurman, R.J.; Kiviat, N.B.; Stoler, M.; **Lorincz, A.T.** (1997) Evaluation of PAPNET testing as an ancillary tool to clarify the status of the "atypical" cervical smear. Mod. Pathol. 10(6):564-571.

Cope, J.U.; Hildesheim, A.; Schiffman, M.H.; Manos, M.M.; **Lörincz, A.T.**; Burk, R.D.; Glass, A.G.; Greer, C.; Buckland, J.; Helgesen, K.; Scott, D.R.; Sherman, M.E.; Kurman, R.J.; Liaw, K.-L. (1997) Comparison of the Hybrid Capture tube test and PCR for detection of human papillomavirus DNA in cervical specimens. J. Clin. Microbiol., 35(9):2262-2265.

Cullen, A.P.; Long, C.D.; **Lörincz, A.T.** (1997) Rapid detection and typing of herpes simplex virus DNA in clinical specimens by the Hybrid Capture II signal amplification probe test. J. Clin. Microbiol. 35(9):2275-2278.

Lörincz, A.T. (1997) Methods of DNA hybridization and their clinical applicability to human papillomavirus detection. In: New Developments in Cervical Cancer Screening and Prevention (Franco, E.; Monsonego, J., eds.), pp. 325-337. Blackwell Science, Oxford.

Herrero, R.; Schiffman, M.H.; Bratti, C.; Hildesheim, A.; Sherman, M.E.; Morales, J.; Mekbel, S.; Alfaro, M.; Balmaceda, I.; Greenberg, M.; **Lorincz, A.** (1997) Evaluation of multiple screening techniques in a high-risk area: the Guanacaste project. In: New Developments in Cervical Cancer Screening and Prevention (Franco, E.; Monsonego, J., eds.), pp. 389-399. Blackwell Science, Oxford.

Chesebro, M.J.; Everett, W.D.; **Lörincz, A.** (1997) High-risk human papillomavirus testing of women with cytological low-grade squamous intraepithelial lesions. J. Lower Genital Tract Dis. 1(4):234-239.

Hildesheim, A..; Schiffman, M.H.; Tsukui, T.; Swanson, C.A.; Lucci, J., III; Scott, D.R.; Glass, A.G.; Rush, B.B.; **Lorincz, A.T.**; Corrigan, A.; Burk, R.D.; Helgesen, K.; Houghten, R.A.; Sherman, M.E.; Kurman, R.J.; Berzofsky, J.A.; Kramer, T.R. (1997) Immune activation in cervical neoplasia: cross-sectional association between plasma soluble interleukin 2 receptor levels and disease. Cancer Epidemiol. Biomarkers Prev. 6(10):807-813.

Ferris, D.G.; Wright, T.C., Jr.; Litaker, M.S.; Richart, R.M.; **Lorincz, A.T.**; Sun, X.-W.; Woodward, L. (1998) Comparison of two tests for detecting carcinogenic HPV in women with Papanicolaou smear reports of ASCUS and LSIL. J. Fam. Pract. 46(2):136-141.

Ferris, D.G.; Wright, T.C., Jr.; Litaker, M.S.; Richart, R.M.; **Lorincz, A.T.**; Sun, X.-W.; Borgatta, L.; Buck, H.; Kramer, L.; Rubin, R. (1998) Triage of women with ASCUS and LSIL on Pap smear reports: management by repeat Pap smear, HPV DNA testing, or colposcopy? J. Fam. Pract. 46(2):125-134.

Lörincz, A.T.; Cullen, A.; Long, C. (1998) Rapid detection and typing of herpes simplex virus DNA in clinical specimens by the Hybrid Capture II signal amplification probe test [Authors' reply to letter to the editor]. J. Clin. Microbiol. 36(3):852.

Wright, T.C., Jr.; **Lorincz, A.**; Ferris, D.G.; Richart, R.M.; Ferenczy, A.; Mielzynska, I.; Borgata, L. (1998) Reflex human papillomavirus DNA testing in women with abnormal Papanicolaou smears. Am. J. Obstet Gynecol. 178(5):962-966.

Lörincz, A. (1998) Hybrid Capture. Clin. Chem. 44(6):1363.

Nindl, I.; **Lörincz, A.**; Mielzynska, I.; Petry, U.; Baur, S.; Kirchmayr, R.; Michels, W.; Schneider, A. (1998) Human papillomavirus detection in cervical intraepithelial neoplasia by a second-generation hybrid capture microplate test, comparing two different cervical specimen collection methods. Clin. Diagn. Virol. 10:49-56.

Lörincz, A.; Davies, P.O. (1998) The Hybrid Capture II Assay for the detection of human papillomavirus. In: Genital Infections and Neoplasia Update. (Monsonego, J., editor), pp 18-19. EUROGIN Scientific Publications, Paris.

Peyton, C.L.; Schiffman, M.; **Lörincz, A.T.**; Hunt, W.C.; Mielzynska, I.; Bratti, C.; Eaton, S.; Hildesheim, A.; Morera, L.A.; Rodriguez, A.C.; Herrero, R.; Sherman, M.E.; Wheeler, C.M. (1998) Comparison of PCR- and Hybrid Capture-based human papillomavirus detection systems using multiple cervical specimen collection strategies. J. Clin. Microbiol. 36(11):3248-3254.

Hildesheim, A.; Schiffman, M.; Scott, D.R.; Marti, D.; Kissner, T.; Sherman, M.E.; Glass, A.G.; Manos, M.M.; **Lorincz, A.T.**; Kurman, R.J.; Buckland, J.; Rush, B.B.; Carrington, M. (1998) Human leukocyte antigen class I/II alleles and development of human papillomavirus-related cervical neoplasia: results from a case-control study conducted in the United States. Cancer Epidemiol. Biomarkers Prev. 7:1035-1041.

Sherman, M.E.; Schiffman, M.; Herrero, R.; Kelly, D.; Bratti, C.; Mango, L.; Alfaro, M.; Hutchinson, M.L.; Mena, F.; Hildesheim, A.; Morales, J.; Greenberg, M.; Balmaceda, I.; **Lorincz, A.T.** (1998) Performance of a semiautomated Papanicolaou smear screening system: results of a population-based study conducted in Guanacaste, Costa Rica. Cancer 84(5):273-280.

Schneider, D.L.; Herrero, R.; Bratti, C.; Greenberg, M.D.; Hildesheim, A.; Sherman, M.E.; Morales, J.; Hutchinson, M.L.; Sedlacek, T.V.; **Lorincz, A.**; Mango, L.; Wacholder, S.; Alfaro, M.; Schiffman, M. (1999) Cervicography screening for cervical cancer among 8460 women in a high-risk population. Am. J. Obstet. Gynecol. 180(2):290-298.

Greenberg, M.D.; Reid, R.; Schiffman, M.; Campion, M.J.; Precop, S.L.; Berman, N.R.; Zemlo, T.; Husain, M.; Herman, G.; Omato, K.H.; **Lorincz, A.T.** (1999) A prospective study of biopsy-confirmed cervical intraepithelial neoplasia grade 1: colposcopic, cytologic, and virologic risk factors for progression. J. Lower Gen. Tract Dis. 3(2):104-110.

Girdner, J.L.; Cullen, A.P.; Salama, T.G.; He, L.; **Lorincz, A.**; Quinn, T.C. (1999) Evaluation of the Digene Hybrid Capture II CT-ID test for the detection of *Chlamydia trachomatis* in female endocervical specimens. J. Clin. Microbiol. 37(5):1579-1581.

Cox, J.T.; Herbst, A.L.; Kinney, W.; **Lörincz, A.T.**; Richart, R.M.; Schiffman, M.H. (1999) Advanced technologies in cervical cancer screening: ASCCP biennial meeting 1998. J. Lower Gen. Tract Dis. 3(suppl 1):S8-S28.

Modarress, K.J.; Cullen, A.P., Jaffurs, W.J., Sr.; Troutman, G.L.; Mousavi, N.; Hubbard, R.A.; Henderson, S., **Lörincz, A.T.** (1999) Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in swab specimens by the Hybrid Capture II and PACE 2 nucleic acid probe tests. Sex. Transm. Dis. 26(5):303-308.

Hutchinson, M.L.; Zahniser, D.J.; Sherman, M.E.; Herrero, R.; Alfaro, M.; Bratti, M.C.; Hildesheim, A.; **Lorincz, A.T.**; Greenberg, M.D.; Morales, J.; Schiffman, M. (1999) Utility of liquid-based cytology for cervical carcinoma screening: results of a population-based study conducted in a region of Costa Rica with a high incidence of cervical carcinoma. Cancer Cytopathol. 87(2):48-55.

Lörincz, A.T. (1999) Human papillomaviruses. In: Lennette E.H., Smith T.F., editors. Laboratory Diagnosis of Viral Infections. 3rd ed. New York: Marcel Dekker; pp. 635-663.

Harper, D.M.; Hildesheim, A.; Cobb, J.L.; Greenberg, M.; Vaught, J.; **Lorincz, A.T.** (1999) Collection devices for human papillomavirus. J. Fam. Pract. 48(7):531-535.

Cuzick, J.; Beverley, E.; Ho, L.; Terry, G.; Sapper, H.; Mielzynska, I. **Lorincz, A.**; Chan, W.-K.; Krausz, T.; Soutter, P. (1999) HPV testing in primary screening of older women. Br. J. Cancer 81(3):554-558.

Serwadda, D.; Wawer, M.J.; Shah, K.V.; Sewankambo, N.K.; Daniel, R.; Li, C.; **Lorincz, A.**; Meehan, M.P.; Wabwire-Mangen, F.; Gray, R.H. (1999) Use of a Hybrid Capture assay of self-collected vaginal swabs in rural Uganda for detection of human papillomavirus. J. Infect. Dis., 180(4):1316-1319.

Lazar, J.G.; Cullen, A.P.; Mielzynska, I.; Meijide, M.G.; **Lörincz, A.T.** (1999) Hybrid Capture®: a sensitive signal amplification-based chemiluminescent test for the detection and quantitation of human viral and bacterial pathogens. J. Clin. Ligand Assay, 22(2):139-151.

Schachter, J.; Hook, E.W., III; McCormack, W.M.; Quinn, T.C.; Chernesky, M.; Chong, S.; Girdner, J.I.; Dixon, P.B.; DeMeo, L.; Williams, E.; Cullen, A.; **Lorincz, A.** (1999) Ability of the Digene Hybrid Capture II

test to identify *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in cervical specimens. J. Clin. Microbiol. 37(11):3668-3671.

Wright, T.C., Jr.; Denny, L.; Kuhn, L.; Pollack, A.; **Lorincz, A.** (2000) HPV DNA testing of self-collected vaginal samples compared with cytologic screening to detect cervical cancer. JAMA 283(1):81-86.

Schiffman, M.; Herrero, R.; Hildesheim, A.; Sherman, M.E.; Bratti, M.; Wacholder, S.; Alfaro, M.; Hutchinson, M.; Morales, J.; Greenberg, M.D.; **Lorincz, A.T.** (2000) HPV DNA testing in cervical cancer screening: results from women in a high-risk province of Costa Rica. JAMA 283(1):87-93.

Kuhn, L.; Denny, L.; Pollack, A.; **Lorincz, A.**; Richart, R.M.; Wright, T.C. (2000) Human papillomavirus DNA testing for cervical cancer screening in low-resource settings. J. Natl. Cancer Inst. 92(10):818-825.

Liaw, K.-L.; Schiffman, M..; Cope, J.U.; Glass, A.G.; Manos, M.M.; Sherman, M.E.; Burk, R.D.; Hildesheim, A.; **Lörincz, A.T.** (2000) Update on recent clinical studies using HPV testing for screening and diagnosis of cervical neoplasia. CME J. Gynecol. Oncol. 5(1):41-44.

Denny, L.; Kuhn, L.; Risi, L.; Richart, R.M.; Pollack, A.; **Lorincz, A.**; Kostecki, F.; Wright, T.C.,Jr. (2000) Two-stage cervical cancer screening: An alternative for resource-poor settings. Am. J. Obstet. Gynecol. 183(2):383-388.

Anthony, J.G.; Linske-O'Connell, L; **Lorincz, A.T.** (2000) Nucleic acid hybridization. In: Specter, S.; Hodinka, R.L.; Young, S.A., editors. Clinical Virology Manual. 3rd ed. Washington, DC: ASM Press, pp. 169-81.

Sellors, J.W.; Mahony, J.B.; Kaczorowski, J.; Lytwyn, A.; Bangura, H.; Chong, S.; **Lorincz, A.**; Dalby, D.M.; Janjusevic, V.; Keller, J.L; for the Survey of HPV in Ontario Women (SHOW) Group. (2000) Prevalence and predictors of human papillomavirus infection in women in Ontario, Canada. Canadian Medical Association Journal 163(5):503-508.

Sellors, J.W.; **Lorincz, A.T.**; Mahony, J.B.; Mielzynska, I.; Lytwyn, A.; Roth, P.; Howard, M.; Chong, S.; Daya, D.; Chapman, W.; Chernesky, M. (2000) Comparison of self-collected vaginal, vulvar and urine samples for human papillomavirus testing to detect high-grade squamous intraepithelial lesions. Canadian Medical Association Journal 163(5):513-518.

Lytwyn, A.; Sellors, J.W.; Mahony, J.B.; Daya, D.; Chapman, W.; Ellis, N.; Roth, P.; **Lorincz, A.T.**; Gafni, A.; for the HPV Effectiveness in Lowgrade Paps (HELP) Study No. 1 Group. (2000) Comparison of human papillomavirus DNA testing and repeat Papanicolaou test in women with low-grade cervical cytologic abnormalities: a randomized trial. Canadian Medical Association Journal 163(6):701-707.

Bozzetti, M.; Nonnenmacher, B.; Mielzynska, I.; Villa, L.; **Lorincz, A.**; Breitenbach, V.; Prolla, J. (2000) Comparison between hybrid capture II and polymerase chain reaction results among women at low risk for cervical cancer. Ann. Epidemiol. 10(7):466.

Belinson, J.; Qiao, Y.; Pretorius, R.; Keaton, K.; Elson, P.; Fischer, C.; **Lorincz, A.**, Zahniser, D.; Wilbur, D.; Pan, Q.; Li, L.; Zhang, W.; Lee, A.; Wu, L.; Ling, Y. Prevalence of cervical cancer and feasibility of screening in rural China: a pilot study for the Shanxi Province Cervical Cancer Screening Study. Manuscript completed.

Pretorius, R.G.; Peterson, P.; Novak, S.; Azizi, F.; Sadeghi, M.; Lorincz, A.T. Comparison of the first and second generation Hybrid Capture tests for high-risk human papillomavirus as an aid to colposcopy. Manuscript completed.

Attachment A

PUBLICATIONS, 1977-1994

Jagadish, M.N., **A.T. Lörincz**, and B.L.A. Carter (1977) Cell size and cell division in yeast cultured at different growth rates. FEMS Microbiol. Lett. 2:235-237.

Carter, B.L.A., **A.T. Lörincz**, and G.C. Johnston (1978) Protein synthesis, cell division and the cell cycle in *Saccharomyces cerevisiae* following a shift to a richer medium. J. Gen. Microbiol. 106:222-225.

Johnston, G.C., C.W. Ehrhardt, **A.T. Lörincz**, and B.L.A. Carter (1979) Regulation of cell size in the yeast *Saccharomyces cerevisiae*. J. Bacteriol. 137:1-5.

Lörincz, A.T. and B.L.A. Carter (1979) Control of cell size at bud initiation in *Saccharomyces cerevisiae*. J. Gen. Microbiol. 113:287-295.

Lörincz, A.T., M.J. Miller, N.-H. Xuong, and E.P. Geiduschek (1982) Identification of proteins whose synthesis is modulated during the cell cycle of *Saccharomyces cerevisiae*. Mol. Cell. Biol. 2:1532-1549.

Lörincz, A.T. and B.L.A. Carter (1983) Cell cycle initiation and bud emergence in *Saccharomyces cerevisiae*. J. Gen. Microbiol. 129:1599-1605.

Lörincz, A.T. and S.I. Reed (1984) Primary structure homology between the product of yeast cell division control gene *CDC 28* and vertebrate oncogenes. Nature 307:183-185.

Reed, S.I., J.A. Hadwiger and **A.T. Lörincz**, (1985) Protein kinase activity associated with the product of the yeast cell division cycle gene *CDC 28*. Proc. Natl. Acad. Sci. USA 82:4055-4059.

Reed, S.I., M.A. deBarros Lopes, J. Ferguson, J.A. Hadwiger, J.-Y. Ho, R. Horwitz, C.A. Jones, **A.T. Lörincz**, M.D. Mendenhall, T.A. Peterson, S. Richardson, and C. Wittenburg (1985) Genetic and molecular analysis of division control in yeast. Cold Spring Harb. Symp. Quant. Biol. 50:627-634.

Lörincz, A.T. and S.I. Reed (1986) Sequence analysis of temperature-sensitive mutations in the *Saccharomyces cerevisiae* gene *CDC 28*. Mol. Cell. Biol. 6:4099-4103.

Lörincz, A.T., W.D. Lancaster, and G.F. Temple (1986) Cloning and characterization of the DNA of a new human papillomavirus from a woman with dysplasia of the uterine cervix. J. Virol. 58:225-229.

Lörincz, A.T., W.D. Lancaster, R.J. Kurman, A.B. Jenson, and G.F. Temple (1986) Characterization of human papillomaviruses in cervical neoplasias and their detection in routine clinical screening. In: Banbury Report 21: Viral Etiology of Cervical Cancer (T. Peto and H. zur Hausen, eds.), pp. 225-237. Cold Spring Harbor Laboratory, New York.

Lörincz, A.T., G.F. Temple, J.A. Patterson, A.B. Jenson, R.J. Kurman, and W.D. Lancaster (1986) Correlation of cellular atypia and human papillomavirus deoxyribonucleic acid sequences in exfoliated cells of the uterine cervix. Obstet. Gynecol. 68:508-512.

Reid. R., M. Greenberg, A.B. Jenson, M. Husain, J. Willett, Y. Daoud, G. Temple, C.R. Stanhope, A.I. Sherman, G.D. Phibbs, and **A.T. Lörincz** (1987) Sexually transmitted papillomaviral infections. I. The anatomic distribution and pathologic grade of neoplastic lesions associated with different viral types. Am. J. Obstet. Gynecol. 156:212-222.

Lörincz, A.T., A.P. Quinn, W.D. Lancaster, and G.F. Temple (1987) A new type of papillomavirus associated with cancer of the uterine cervix. Virol. 159:187-190.

Lörincz, A.T (1987) Detection of human papillomavirus infection by nucleic acid hybridization. In: Obstetrics and Gynecology Clinics of North America (Reid, R., ed.), vol. 14, pp. 451-469. W.B. Saunders, Philadelphia.

Lörincz, A.T., G.F. Temple, R.J. Kurman, A.B. Jenson, and W.D. Lancaster (1987) Oncogenic association of specific human papillomavirus types with cervical neoplasia. J. Natl. Canc. Inst. 79:671-677.

Naghashfar, Z.S., N.B. Rosenshein, **A.T. Lörincz**, J. Buscema, and K.V. Shah (1987) Characterization of human papillomavirus type 45, a new type 18-related virus of the genital tract. J. Gen. Virol. 68:3073-3079

Barnes, W., G. Delgado, R.J. Kurman, E.S. Petrilli. D.M. Smith, S. Ahmed, **A.T. Lörincz**, G.F. Temple, A.B. Jenson, and W.D. Lancaster (1988) Possible prognostic significance of human papillomavirus type in cervical cancer. Gynecol. Oncol. 29:267-273.

Kurman R.J., M.H. Schiffman, W.D. Lancaster, R. Reid, A.B. Jenson, G.F. Temple and **A.T. Lörincz** (1988) Analysis of individual human papillomavirus types in cervical neoplasia. A possible role for type 18 in rapid progression. Am. J. Obstet. Gynecol. 159:293-296.

Shimoda K., **A.T. Lörincz**, G.F. Temple, and W.D. Lancaster (1988) Human papillomavirus type 52: a new virus associated with cervical neoplasia. J. Gen. Virol. 69:2925-2928.

Rosemberg, S.K., R. Reid, M. Greenberg, and **A.T. Lörincz** (1988) Sexually transmitted papillomaviral infection in the male: the urethral reservoir. Urology 32:47-49.

Schachter, J., J. Moncada, C.R. Dawson, S. Sheppard, P. Courtright, M.E. Said, S. Zaki, S.F. Hafez, and **A.T. Lörincz** (1988) Nonculture methods for diagnosing chlamydial infection in patients with trachoma: a clue to the pathogenesis of the disease. J. Infect. Dis. 158:1347-1352.

Willett, G.D., R.J. Kurman, R. Reid, M. Greenberg, A.B. Jenson, and **A.T. Lörincz** (1989) Correlation of the histologic appearance of intraepithelial neoplasia of the cervix with human papillomavirus types: emphasis on low grade lesions including so-called flat condyloma. Int. J. Gynecol. Pathol. 8:18-25.

Lörincz, A.T., A.P. Quinn, M.D. Goldsborough, B.J. Schmidt, and G.F. Temple (1989) Cloning and partial DNA sequencing of two new human papillomavirus types associated with condylomas and low-grade cervical neoplasia. J. Virol. 63:2829-2834.

Goldsborough, M.D., D. DiSilvestre, G.F. Temple, and **A.T. Lörincz** (1989) Nucleotide sequence of human papillomavirus type 31: a cervical neoplasia-associated virus. Virol. 171:306-311.

Lörincz, A.T., A.P. Quinn, M.D. Goldsborough, P. McAllister, and G.F. Temple (1989) Human papillomavirus type 56: a new virus detected in cervical cancers. J. Gen. Virol. 70:3099-3104.

Lörincz, A.T. and R. Reid (1989) The association of human papillomavirus with gynecologic cancer. Curr. Opinion Oncol. 1:123-132.

Lörincz, A.T. (1989) Human papillomavirus testing. Diag. Clin. Test. 27:28-37.

Lörincz, A.T. (1990) Human papillomavirus detection tests. In: Sexually Transmitted Diseases, 2nd edition (Holmes, K.K., et al., eds.), pp. 953-959. McGraw-Hill, New York.

Lörincz, A.T., M.H. Schiffman, W.J. Jaffurs, J. Marlow, A.P. Quinn, and G.F. Temple (1990) Temporal associations of human papillomavirus infection with cervical cytological abnormalities. Am. J. Obstet. Gynecol. 162:645-651.

Reid, R., M.D. Greenberg, **A.T. Lörincz**, Y. Daoud, D. Pizzuti, and M. Stoler (1990) Superficial laser vulvectomy. IV. Extended laser vaporization and adjunctive 5-fluorouracil therapy of human papillomavirus associated vulvar disease. Obstet. Gynecol. 76:439-448.

Cullen, A.P., R. Reid, M. Campion, and **A.T. Lörincz** (1991) Analysis of the physical state of different human papillomavirus DNAs in preinvasive and invasive cervical neoplasms. J. Virol. 65:606-612.

Schiffman, M.H., H.M. Bauer, **A.T. Lörincz**, M.M. Manos, J.C. Byrne, A.G. Glass, D.M. Cadell, and P.M. Howley (1991) Comparison of Southern blot hybridization and polymerase chain reaction methods for detection of human papillomavirus DNA. J. Clin. Microbiol. 29:573-577.

Reid, R., M.D. Greenberg, **A.T. Lörincz**, A.B. Jenson, C.R. Laverty, M.D. Husain, Y. Daoud, B. Zado, T. White, D. Cantor, and M. Goldrath (1991) Should cervical cytologic testing be augmented by cervicography or human papillomavirus deoxyribonucleic acid detection? Am. J. Obstet. Gynecol. 164:1461-1471.

Reid, R. and **A.T. Lörincz** (1991) Should family physicians test for human papillomavirus infection? An affirmative view. J. Fam. Pract. 32:1-10.

Nasseri, M., J.R. Gage, **A. Lörincz**, and F.O. Wettstein (1991) Human papillomavirus type 16 immortalized cervical keratinocytes contain transcripts encoding E6, E7, and E2 initiated at the p97 promoter and express high levels of E7. Virology 184:131-140.

Lörincz, A (1991) Detection of sexually transmitted pathogens with nucleic acid techniques. Ups. J. Med. Sci. Suppl. 50:39-41.

Lörincz, A.T., R. Reid, A.B. Jenson, M.D. Greenberg, W.D. Lancaster, and R.J. Kurman (1992) Human papillomavirus infection of the cervix: relative risk associations of 15 common anogenital types. Obstet. Gynecol. 79:328-337.

Chapman, W.B., **A.T. Lörincz**, G.D. Willett, V.C. Wright, and R.J. Kurman (1992) Epidermal growth factor receptor expression and the presence of human papillomavirus in cervical squamous intraepithelial lesions. Int. J. Gynecol. Pathol. 11:221-226.

Kiviat, N.B., L.A. Koutsky, C.W. Critchlow, **A.T. Lörincz**, A.P. Cullen, J. Brockway and K.K. Holmes (1992) Prevalence and cytologic manifestations of human papillomavirus (HPV) types 6, 11, 16, 18, 31, 33, 35, 42, 43, 44, 45, 51, 52 and 56 among 500 consecutive women. Int. J. Gynecol. Pathol. 11:197-203.

Lörincz, A (1992) Nucleic acid hybridization. In: Clinical Virology Manual, 2nd edition (Lancz G. and S. Specter, eds.), pp. 285-298. Elsevier, New York.

Lörincz A (1992) Detection of human papillomavirus DNA without amplification: prospects for clinical utility. In: IARC Scientific Publication No. 119: Human Papilloma Virus and Cervical Cancer (N. Munoz and F.X. Bosch, eds.), pp. 135-145. Oxford University Press, Oxford UK.

Goldsborough, M.D., P. McAllister, R. Reid, G. Temple, and **A.T. Lörincz** (1992) A comparison study of human papillomavirus prevalence by the polymerase chain reaction in low risk women and in a gynecology referral group at elevated risk for cervical cancer. Mol. Cell. Probes 6:451-457.

Munoz, N., F.X. Bosch, S. de Sanjose, L. Tafur, I. Izarzugaza, M. Gili, P. Viladiu, C. Navarro, C. Martos, N. Ascunce, L.C. Gonzalez, J.M. Kaldor, E. Guerrero, **A. Lörincz**, M. Santamaria, P. Alonso de Ruiz, N. Aristizabal, and K. Shah (1992) The causal link between human papillomavirus and invasive cervical cancer: a population-based case-control study in Columbia and Spain. Int. J. Cancer 52:743-749.

Lörincz, A (1992) Diagnosis of human papillomavirus infection by the new generation of molecular DNA assays. Clin. Immunol. Newslett. 12:123-128.

Chapman, W.B., **A.T. Lörincz**, G.D. Willett, V.C. Wright, and R.J. Kurman (1993) Evaluation of two commercially available *in situ* hybridization kits for detection of human papillomavirus DNA in cervical biopsies: comparison to Southern blot hybridization. Mod. Pathol. 6:73-79.

Kessis, T.D., R.J. Slebos, W.G. Nelson, M.B. Kastan, B.S. Plunkett, S.M. Han, **A.T. Lörincz**, L. Hedrick, and K.R. Cho (1993) Human papillomavirus 16 E6 expression disrupts the p53-mediated cellular response to DNA damage. Proc. Natl. Acad. Sci. USA 90:3988-3992.

Sherman, M.E., M.H. Schiffman, **A.T. Lorincz**, M.M. Manos, D.R. Scott, R.J. Kurman, N.B. Kiviat, M. Stoler, A.G. Glass, and B.B. Rush (1994) Towards objective quality assurance in cervical cytopathology: correlation of cytopathologic diagnoses with detection of high-risk human papillomavirus types. Am. J. Pathol. 102:182-187.

Attachment B

INVITED SPEAKER
INTERNATIONAL CONFERENCES

1. Bay Area Yeast Meeting. August 3, 1983. Berkeley, California.
2. Origin of Female Genital Cancer. April 14-17, 1985. Cold Spring Harbor, New York.
3. Workshop on Mechanisms of Transformation by Papillomaviruses. February 18-19, 1986. Bethesda, Maryland.
4. Colposcopy, Cervical and Vulvar Pathology and Gynecologic Laser Surgery Conference. April 4-10, 1986. Sarasota, Florida.
5. Human Papillomaviruses and Cervical Carcinoma. Second International Conference. October 27-29, 1986. Chicago, Illinois.
6. Human Papillomaviral Infection and Lower Genital Tract Neoplasia. May 7-9, 1987. Atlanta, Georgia.
7. HPV Workshop - Type Consensus Meeting. March 22-23, 1988. New York, New York.
8. Human Papillomaviruses and Squamous Carcinoma. Third International Conference. October 24-26, 1988. Chicago, Illinois.
9. Impact of HPV Testing on Cervical Cancer Screening and Diagnosis. National Cancer Institute Sponsored Conference. February 2, 1989. Rockville, Maryland.
10. Colposcopy, Cervical and Vulvar Pathology and Gynecologic Laser Surgery Conference. February 27-March 5, 1989. Sarasota, Florida.
11. UCLA Conference on Papillomaviruses. March 11-18, 1989. Taos, New Mexico.
12. An Update: Human Papillomavirus Infection. April 14, 1989. Lenexa, Kansas.
13. Fifth Annual Clinical Virology Symposium. April 30-May 3, 1989. Clearwater Beach, Florida.
14. Thirtieth Annual Meeting of the Japanese Clinical Cytology Society. June 14-16, 1989. Tokyo, Japan.
15. Colposcopy, Cervical and Vulvar Pathology and Gynecologic Laser Surgery Conference. November 5-12, 1989. Sarasota, Florida.
16. Human Papillomavirus Infections—A Postgraduate Course. October 21-22, 1989. Washington, DC.
17. Diagnosis and Treatment of Vulvar, Vaginal and Cervical Disease - A Postgraduate Course. October 27-28, 1989. Washington, DC.
18. National Meeting of the Canadian Association for Clinical Microbiology and Infectious Diseases. November 26-30, 1989. Montreal, Canada.
19. Workshop on Development of STD Diagnostics for Resource-Poor Settings. February 7-8, 1990. Rosslyn, Virginia.
20. Sixth Meeting of the Scandinavian Society for Gynecological Medicine. September 6-8th, 1990. Mariehamn, Finland.
21. International Symposium on Diagnosis of Sexually Transmitted Diseases. August 16-17, 1991. Uppsala, Sweden.
22. Fourth International Conference on Human Papillomaviruses and Genital Carcinoma. September 17-19, 1990. Chicago, Illinois.
23. Second IARC Workshop on HPV and Cervical Cancer, November 25-28, 1991. Brussels, Belgium.
24. Fifth International Conference on Human Papillomavirus. October 25-28, 1992. Chicago, Illinois.
25. St. Joseph's Institute of Laboratory Medicine Symposium. April 29, 1993. London, Ontario, Canada.
26. Twelfth Annual High Technology R&D Trade Fair. May 10-11, 1993. Arlington, Virginia.
27. 8th World Congress of Cervical Pathology and Colposcopy. May 12-16, 1993. Chicago, Illinois.
28. 1993 U.K. Wellcozyme Users Conference. June 17-18, 1993. St. Albans, England.

29. Steering Committee Meeting of the International Biological Study on Cervical Cancer. October 2, 1993. Baltimore, Maryland.
30. The American Society for Colposcopy and Cervical Pathology, in joint sponsorship with The Society of Canadian Colposcopists. March 22-26, 1994. Orlando, Florida.
31. 2nd International Congress of Papillomavirus in Human Pathology. April 6-8, 1994. Paris, France.
32. Novel Amplification Technologies for DNA/RNA-Based Diagnostics. April 20-22, 1994. San Francisco, California.
33. First Congress on Papillomavirus of the Catholic Cancer Center. May 7, 1994. Seoul, Korea.
34. The Feasibility of Genetic Technology to Close the HIV Window in Donor Screening (US FDA workshop) September 26-28, 1994. Silver Spring, Maryland.
35. Nucleic Acid-Based Technology: Revolution in Clinical Diagnosis, Applications and Research. November 7-9, 1994. Amsterdam, The Netherlands.
36. Nucleic Acid-Based Technologies: Current Challenges, Future Strategies, and End User Perspectives. May 31-June 2, 1995. San Francisco, California.
37. Murex Users' Meeting. June 7-8, 1995. London, United Kingdom.
38. Eleventh Meeting of the International Society for STD Research, August 27-30,1995. New Orleans, Louisiana.
39. X Congresso Brasileiro - II Congresso Latino Americano de Patologia do Trato Genital Inferior e Colposcopia. September 20-24, 1995. Sao Paulo, Brazil.
40. Workshop organized by Murex Diagnostica GmbH. October 12, 1995. Zurich, Switzerland.
41. XVth Asian and Oceanic Congress of Obstetrics and Gynecology. October 15-20, 1995. Bali, Indonesia.
42. Gene Quantification: Diagnosis, Monitoring & Drug Development. February 26-27, 1996. San Diego, California.
43. VIII Curso Internacional de Cancer Cervico Uterino y Lesiones Premalignas. March 7-9, 1996. Mexico City, Mexico.
44. Gene Detection: Diagnostic Technology for Infectious Agents and Human Genetic Diseases. May 2-3, 1996. Coronado, California.
45. 9th World Congress of Cervical Pathology and Colposcopy. May 12-16, 1996. Sydney, Australia.
46. EUROGIN-WHO International Joint Experts Meeting "Cervical Cancer Screening and New Developments. June 17-19, 1996. Geneva, Switzerland.
47. State of Maryland Department of Health and Mental Hygiene Office of Maternal Health and Family Planning. August 9, 1996. Annapolis, MD.
48. Advances in Nucleic Acid Amplification & Detection. September 18-19, 1996. Amsterdam, The Netherlands.
49. IV Simposio International e III Jornada Baiana de Patologia do Trato Genital Inferior e Colposcopia. October 3-6, 1996. Salvador, Brazil.
50. The American Society for Microbiology, New York City Branch, & St. John's University. November 1, 1996. Jamaica, New York.
51. XIII Latin American Microbiology Congress. November 5-9, 1996. Caracas, Venezuela.
52. Workshop on Cervical Cancer Screening Program. November 6-7, 1996. Juquei, SP, Brazil.
53. EUROGIN-WHO 3rd International Congress on Lower Genital Tract Infections and Neoplasia: Future Challenges and Strategies. March 25-28, 1997. Paris, France.
54. 15th Annual Reproductive Health Update, co-sponsored by the Maryland Department of Health and Mental Hygiene Office of Maternal Health and Family Planning, Anne Arundel Community College, and Planned Parenthood. April 25, 1997. Arnold, MD.
55. Symposium on HPV Infection and Cervical Cancer. May 11, 1997. Seoul, Korea.
56. HPV workshop. May 16, 1997. Taipei, Taiwan, R.O.C.
57. XV FIGO World Congress of Gynecology and Obstetrics. August 3-8, 1997. Copenhagen, Denmark.

58. HPV Testing: European Perspectives on Cervical Neoplasia Prevention, Prognosis and Management. November 13-15, 1997. Geneva, Switzerland.
59. European HPV Clinical Summit Meeting. January 29-30, 1998. Vienna, Austria.
60. IV Reunión Nacional de Colposcopia y Patologia Cervical. February 19-21, 1998. Guadalajara, Mexico.
61. Gene Quantification: Clinical Applications and Drug Development. March 30-April 1, 1998. San Diego, CA.
62. Biennial Meeting, American Society for Colposcopy and Cervical Pathology. March 30-April 2, 1998. Scottsdale, AZ.
63. ASCP/CAP Spring Meeting. April 4-8, 1998. Los Angeles, CA.
64. 8th European Course on HPV-Associated Pathology. April 22-24, 1998. Munich, Germany.
65. DNA/RNA Diagnostics. May 19-21, 1998. Washington, DC.
66. Microbial-Linked Diseases: Shifting the Pathogenic Paradigm. June 25-26, 1998. San Diego, CA.
67. Human Papillomavirus Infections and Cervical Cancer. July 7-11, 1998. Montreal, Canada.
68. Simposio Internacional sobre HPV: IV Curso de Atualizacao em Patologia do Trato Genital Preparatorio para Concurso de Qualificacao em Colposcopia. September 3-4, 1998. Belo Horizonte, Brazil.
69. IIIer Congreso Lainoamericano y IIdo Congreso Paraguayo de Patologia del Tracto Genital Inferior y Colposcopia. September 7-11, 1998. Asuncion, Paraguay.
70. 17th International Papillomavirus Conference. January 9-15, 1999. Charleston, SC.
71. INCGC - Consensus Conference on Cervical Cancer Screening and Management. January 28-31, 1999. Tunis, Tunisia.
72. HPV Summit 1999: New Approaches to the Detection and Elimination of Cervical Cancer. February 8-10, 1999. Chamonix, France.
73. Centers for Disease Control and Prevention and American Cancer Society External Consultants' Meeting: Prevention of Genital HPV Infection and Sequelae. April 13-14, 1999. Atlanta, GA.
74. 11th International Meeting of Gynaecological Oncology. May 8-12, 1999. Budapest, Hungary.
75. 4th Scientific Meeting on Primary and Secondary Prevention of Gynecological Cancer. May 14-16, 1999. Thessaloniki, Greece.
76. 13th Meeting of the International Society for Sexually Transmitted Diseases Research. July 11-14, 1999. Denver, CO.
77. Reproductive Health '99. September 22-25, 1999. New York. NY.
78. 1999 ASCP/CAP Fall Meeting. September 25-30, 1999. New Orleans, LA.
79. 10th World Congress of Cervical Pathology & Colposcopy. November 7-11, 1999. Buenos Aires, Argentina.
80. North American Sexual Health Management Symposium. November 21-23, 1999. New York, NY.
81. Cervical and Breast Cancer in the Next Millenium. December 3-6, 1999. Mexico City, Mexico.
82. XI Encontro de Atualização em Patologia do Trato Genital Inferior e Colposcopia – Cervicolp' 2000. March 23-25, 2000. Sao Paulo, Brazil.
83. EUROGIN 2000: Global Challenge of Cervical Cancer Prevention. April 4-9, 2000. Paris, France.
84. ASCP/CAP Spring Meeting. April 9-12, 2000. Boston, MA.
85. Clinical Implications Conference 1: "Role of Human Papillomavirus in Cervical Neoplasia." April 28-29, 2000. Chicago, IL.
86. 26th National Meeting of the Clinical Ligand Assay Society. May 31-June 2, 2000. Boston, MA.
87. Meeting of the Pathological Society of Great Britain and Ireland. July 12-14, 2000. Nottingham, UK.
88. 7th International Meeting of Genital Tract Pathology & Colposcopy. October 25-30, 2000. Belo Horizonte, Brazil.

Attachment C

INVITED SPEAKER
DEPARTMENTAL SEMINARS

1. Heidelberg Cancer Research Center, Heidelberg, Germany, November, 1985.
2. Columbia Hospital for Women, Washington, DC, December, 1985, 1986, and 1991.
3. Fred Hutchinson Cancer Research Center, Seattle, Washington, July, 1988.
4. Johns Hopkins Medical Institutions, Baltimore, Maryland, November, 1990.
5. University of New Hampshire, Department of Microbiology, October, 1991.
6. Sharp Memorial Hospital OB/GYN Department, San Diego, California, November 11, 1993.
7. Prodia Laboratory, Jakarta, Indonesia, May 3, 1994.
8. Bio-Check Laboratories Ltd. Pathology, Diagnostic Virus, and Gynecology Departments, Taipei, Taiwan, R.O.C., May 5, 1994.
9. University College Hospital Virology Department, London, United Kingdom, June 16, 1995.
10. John Radcliffe Infirmary Pathology Department, Oxford, United Kingdom, June 17, 1995.
11. National Cancer Hospital Cytology Department, Oslo, Norway, October 10, 1995.
12. Columbia Hospital for Women Pathology Department, Washington, DC, October 24, 1995.
13. Associated Regional University Pathologists (ARUP), Salt Lake City, UT, February 28, 1996.
14. Washington Hospital Center, Transplant Surgery Department, March, 1996.
15. Health Insurance Plan of New York, Jericho, NY, April 24, 1996.
16. Friedrich Schiller University Department of Obstetrics and Gynecology, Jena, Germany, May 8, 1996.
17. Unilab KPT/ Murex Diagnostica GmbH, HPV workshop for gynecologists/venerologists/ pathologists/virologists, Budapest, Hungary, May 10, 1996.
18. Long Island Jewish Medical Center Gynecology Department, New York, NY, June 5, 1996.
19. Washington Gynecological Society, Washington, DC, January 8, 1997.
20. Hyundei Medical Center, Seoul, Korea, May 10, 1997.
21. Seoul National University, Seoul, Korea, May 12, 1997.
22. Papanicolaou Institute, Buenos Aires, Argentina, July 14-16, 1997.
23. Doctors' meeting convened by Murex Central Europe, Vienna, Austria, November 17, 1997.
24. One seminar and one grand rounds, for the departments of Gynecologic Oncology, Biochemistry & Molecular Genetics, and Infectious Diseases at the University of Alabama at Birmingham, December 9-10, 1998.
25. Maryland Bioscience Alliance, High Technology Council of Maryland, Rockville, MD, January 21, 1999.
26. University of Rochester Research Symposium on Human Papillomavirus Infections from the Bench to the Bedside, Rochester, NY, April 30, 1999.
27. Women's Health Task Force Meeting, Washington, DC, February 29-March 1, 2000.
28. Maryland Bioscience Alliance Cancer Forum, High Technology Council of Maryland, Rockville, MD, March 22, 2000.
29. Gynecologic Cancer Translational Research Retreat, Chantilly, VA. May 5-6, 2000.
30. 18th Annual Reproductive Health Update for the Maryland Department of Health, Annapolis, MD. May 19, 2000.
31. Georgetown University Department of Pathology, Washington, DC. May 25, 2000.
32. Cleveland Clinic Foundation, Cleveland, OH. June 30, 2000.

33. University of Medicine and Dentistry of New Jersey, Scotch Plains, NJ. October 13, 2000.